Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 42, 43, 45-97, 103-126 and 130-149 are pending in the application, with claims 42, 48, 58, 64, 69, 75, 85, 91, 97, 139, 142, 145, 146 and 147 being the independent claims. Claims 44, 98-102 and 127-129 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 130-149 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Support for Amended and New Claims

Support for amended claims 42, 47, 48, 57, 58, 63, 64, 68, 69, 74, 82-84, 88-90, 91, 96 and 97, and new claims 131-136 and 147-149 can be found throughout the specification, for example, at page 10, lines 14-33. Support for amended claims 50, 75, 85 and 92 can be found throughout the specification, for example, at page 17, lines 11-12 and in claims 1, 19 and 26 as originally filed. Support for amended claim 51 can be found throughout the specification, for example, at page 16, lines 25-26. Support for amended claims 79-81 can be found throughout the specification, for example, at page 17, lines 29-32. Support for amended claims 118-123 can be found throughout the specification, for example, at page 10,

lines 18-23. Support for new claim 130 can be found throughout the specification, for example, at page 14, lines 21-23. Support for new claims 137-144 can be found throughout the specification, for example, at page 6, line 25 through page 7, line 3, at page 7, lines 18-23, and at page 14, lines 18-23. Support for new claims 145 and 146 can be found throughout the specification, for example, at page 32, lines 14-20.

II. Claim Objections

A. Objection to Claims 42, 97-102 and 127-129

According to the Examiner, claims 42, 97-102 and 127-129 should begin with an article. *See* Paper No. 16, page 2. Applicants respectfully traverse this objection. Applicants submit that all of the currently pending claims are in full compliance with the requirements of 37 C.F.R. § 1.75 and that no amendment to the form of the claims is required. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this objection.

B. Objection to Claim 50

According to the Examiner, "[c]laim 50 recites the term 'endogenous vectors'; however, it appears that the term should read 'endogenous plasmids'." Paper No. 16, page 2. Applicants have amended claim 50 to recite "endogenous plasmids." Thus, the objection to claim 50 has been fully accommodated and should be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 42-129 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. *See* Paper No. 16, pages 2-3. The Examiner has put forth two separate bases for this rejection, each of which is addressed in turn below.

A. The Inclusion of "Strain C"

With respect to claims 43, 49, 50, 59, 60, 65, 70, 71, 93 and 99, the Examiner stated:

> Applicant indicates the use of strain C as a limitation of these claims, but has not adequately described the strain in the specification so that the skilled artisan would know how to use the strain, or even if he possessed the strain. Applicant has not indicated the nature of strain C in terms of how to make this strain, what the genotype of the strain is, or where the strain is available in terms of a deposit number.

Paper No. 16, page 3. Applicants respectfully disagree with the Examiner's assertion and traverse this basis of the rejection.

A person of ordinary skill in the art would recognize that Applicants were in possession of *E. coli* strain C. Strain C is disclosed in several places throughout the specification. *See, e.g.*, page 14, lines 20-23, page 33, lines 20-22, and page 38, last strain listed in Table 1 (describing the relevant genetic markers of an *E. coli* strain C clone designated BRL 3229). In addition, Applicants note that *E. coli* strain C is a strain that has been well known to those of ordinary skill in the art for many years. *See, e.g.*, Bertani and

Weigle, *J. Bacteriol. 65*:113-121 (1953) (copy attached hereto as Exhibit 1) (identifying *E. coli* strain C as "no. 122 of the National Collection of Type Cultures, London"); *see also* Sambrook *et al.*, "Bacterial Strain List, Table A.2" in *Molecular Cloning, A Laboratory Manual*, Sambrook *et al.*, eds., Cold Spring Harbor Laboratory Press, p. A.9 (1989) (copy attached hereto as Exhibit 2) (noting that "*E. coli* strain C is F^- and lacks host restriction and modification activity. It is a nonsuppressing host strain used in complementation tests with amber mutants of bacteriophage λ."). Moreover, a clone of strain C, designated C-1a, can be obtained from the *E. coli* genetic stock center at Yale University as strain CGSC No. 3121. *See* CGSC strain designation summary for *E. coli* strain C-1a (copy attached hereto as Exhibit 3).

Thus, a person of ordinary skill in the art would appreciate the nature and characteristics of *E. coli* strain C and would clearly recognize that Applicants were in possession of the invention insofar as it relates to *E. coli* strain C. Applicants therefore respectfully request that the first basis of the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

B. E. coli Having a Growth Rate that is at Least 5% Greater

The second basis for the rejection under § 112, first paragraph, is the Examiner's assertion that:

> as applicant has only disclosed a written description for the indicated strain (ATCC 9637) and derivatives generated from the strain, and not for a representative number of strains through specific identifying characteristics, they have not satisfied the written description requirement to show the

> skilled artisan that they were in possession of the claimed genus.

Paper No. 16, page 4. Applicants respectfully traverse this basis for the rejection.

A person of ordinary skill in the art would have appreciated that Applicants were in possession of the claimed genus of *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B, as well as the claimed compositions and methods that include or involve the use of such *E. coli*.

The written description requirement for a claimed genus can be satisfied, *e.g.*, by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that the Applicant was in possession of the claimed genus. *See Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The Federal Circuit has recently indicated that functional descriptions may satisfy the written description requirement. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002) ("It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement.") The principle inquiry is whether the disclosed functional characteristics are coupled with a known or disclosed correlation between function and structure; if so, the written description requirement is satisfied. *See id.*

Applicants have described in the present specification that the *E. coli* of the invention have a growth rate that is at least 5% greater than the growth rate of at least one

microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B. *See, e.g.*, specification at page 10, lines 14-25. The specification teaches that the *E. coli* of the invention can be identified in terms of, *e.g.*, time to colony formation and/or doubling time. *See id.* at page 14, lines 31-32. The specification also describes the growth rate (in terms of time to 1 mm colony size) of several exemplary clones derived from *E. coli* W. *See* specification at pages 39-40, Tables 2-4. Thus, a skilled artisan could have readily ascertained whether a given *E. coli* is encompassed by or included within the claimed invention.

Moreover, as of the effective filing date of the application, the genetics and molecular biology of *E. coli* were well established in the art. Thus, a skilled artisan could have easily ascertained the physical (*i.e.*, "structural") attributes of the *E. coli* of the invention, including their genetic characteristics. A skilled artisan could have also correlated such genetic characteristics with the functional characteristics of the *E. coli* (*i.e.*, having a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294, DH5α or DH10B). In view of this correlation between "structure" and "function" in *E. coli*, and the exemplary rapid growing *E. coli* presented in the specification, it would have been concluded by persons of ordinary skill in the art that Applicants were in possession of the subject matter encompassed by the present claims.

Applicants also note that claims 43, 49, 59, 60, 65, 70 and 93 (as well as new claims 130, 139 and 142) specify that the *E. coli* of these claims are *E. coli* strain W or strain C. New claims 145 and 146 specify that the claimed *E. coli* have deposit numbers NRRL B-30143 and NRRL B-30144, respectively. Thus, the Examiner's explanation for the second

basis of the rejection under § 112, first paragraph, *i.e.*, that the claims "encompass all strains that have growth rates that are at least 5% greater than those of the reference microorganism," cannot apply to these claims.

In view of the foregoing, Applicants respectfully request that the second basis of rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

IV. Claim Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 51 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Paper No. 16, page 5. It is stated in the Office Action that there is insufficient antecedent basis for the expression "recombinant vector" in claim 51. Solely to expedite prosecution, Applicants have amended claim 51 to recite "vector" rather than "recombinant vector." Thus, the rejection under 35 U.S.C. § 112, second paragraph, has been fully accommodated and should be withdrawn.

V. Claim Rejections Under 35 U.S.C. § 102

Claims 75, 82-85, 88-90 and 118-123 were rejected under 35 U.S.C. § 102(b) based on the asserted prior commercial availability of *E. coli* strain W (ATCC 9637). *See* Paper No. 16, page 5.

Under 35 USC § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983). Claims 75 and 85 have been amended to

specify that the *E. coli* of the claimed kits and compositions lack endogenous plasmids. The *E. coli* strain designated ATCC 9637 contains endogenous plasmids. *See* specification at page 20, lines 23-24. Thus, the asserted prior commercial availability of ATCC 9637 cannot anticipate claims 75, 82-85, 88-90 and 118-123 in their present form. Applicants therefore respectfully request that the rejection of these claims under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

VI. Claim Rejections Under 35 U.S.C. § 103

A. E. coli Strain W in View of Trevors

Claims 42, 43, 45-47 and 103-105 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over "applicant's admissions concerning *E. coli* strain W[1]" in view of Trevors, *FEMS Microbiol. Rev. 32*:149-157 (1986) (hereinafter "Trevors"). *See* Paper No. 16, page 7. Applicants respectfully traverse this rejection.

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the references or to combine reference teachings. *See In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). The evidence demonstrating a motivation to combine references must be "clear and particular." *See In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). "Broad

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[1]The Examiner described this rejection (as well as all the remaining rejections under § 103) as being based, in part, on "applicant's admissions concerning *E. coli* strain W." Applicants' own statements set forth in the specification, however, cannot properly be regarded as part of the prior art. It appears that the Examiner intended the rejections under § 103 to be based on the asserted prior commercial availability of *E. coli* strain W, as described in the rejection under § 102, in view of Applicants' statements in the specification regarding the growth rate of *E. coli* strain W and the other cited references.

conclusory statements regarding the teaching of multiple references, standing alone, are not 'evidence.'" *Id.*, 175 F.3d at 999, 50 USPQ2d at 1617. Here, the Examiner has not presented any specific evidence as to why a skilled artisan would be motivated to modify *E. coli* strain W based on the teachings of Trevors. Thus, a *prima facie* case of obviousness has not been established.

Claims 42, 43, 45-47 and 103-105 are directed to isolated *E. coli* lacking endogenous plasmids and having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

There is no suggestion in the art to modify *E. coli* strain W (or any other rapid growing microorganism) so that it lacks endogenous plasmids. Trevors simply provides a general overview of various plasmid curing agents and procedures. *See* Trevors at page 149, top right column. There is no disclosure of *E. coli* W or of rapid growing *E. coli* in Trevors at all. The Examiner, however, stated that:

> [t]he ordinary skilled artisan would have been motivated to apply the teachings of Trevors to *E. coli* strain W in order to obtain a strain that was unhindered in growth by the replication of extra DNA (plasmids), and which did not contain plasmids that could potentially interfere with biotechnological applications (cloning/plasmid recovery, etc.). It would have been obvious to apply Trevors to *E. coli* strain W because the method of Trevors is directed to a bacterial strain harboring plasmids, which *E. coli* strain W represents.

Paper No. 16, page 8.

Applicants respectfully submit that the Examiner's justification for the rejection under 35 U.S.C. § 103 is legally insufficient. Trevors does not indicate or suggest that the

replication of *E. coli* is hindered in growth by "extra DNA." Nor does Trevors indicate or suggest that plasmids could "potentially interfere with biotechnological applications." Trevors simply states that obtaining a plasmid-cured derivative "allows a direct comparison to be made between the plasmid-containing and plasmid-cured cells." Trevors at page 149, left column. Importantly, there is no suggestion in Trevors that the plasmid curing agents and procedures mentioned therein could or should be applied to *E. coli* strain W or to any rapid growing *E. coli*. In addition, the mere fact that the agents and procedures in Trevors relate to bacterial strains harboring plasmids does not constitute sufficient motivation to apply such agents and procedures *specifically* to *E. coli* strain W.

In sum, Trevors does not provide any specific motivation for the production of *E. coli* cells that lack endogenous plasmids and that have a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294, DH5α or DH10B. Thus, a *prima facie* case of obviousness has not been established. *E. coli* strain W in view of Trevors does not render any of the currently presented claims, including the newly added claims, obvious. Accordingly, Applicants respectfully request that the rejection of claims 42, 43, 45-47 and 103-105 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

B. E. coli Strain W in View of Jessee

Claims 48, 49, 51, 55-57, 69, 70, 72-74, 76-81, 86, 87, 91, 93-97, 99-102, 106-108, 115-117 and 124-129 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over "applicant's admissions concerning *E. coli* strain W" in view of Jessee *et*

al., U.S. Patent No. 4,981,797 (hereinafter "Jessee"). *See* Paper No. 16, page 9. Applicants respectfully traverse this rejection.

1. Claims 48, 49, 51, 55-57, 69, 70, 72-74, 91, 93-97, 99-102, 106-108, 115-117 and 124-129

Claims 48, 49, 51, 55-57 and 106-108 are directed to methods of cloning comprising: (a) obtaining competent *E. coli*; (b) transforming said competent *E. coli* with at least one vector; (c) selecting transformed *E. coli* containing said at least one vector; and (d) culturing said transformed *E. coli*; wherein said *E. coli* are *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

Claims 69, 70, 72-74 and 115-117 are directed to methods of transforming *E. coli*, comprising: (a) obtaining competent *E. coli*; (b) incubating said *E. coli* in the presence of one or more vectors under conditions which cause said one or more vectors to be taken up by said *E. coli*; and (c) culturing said *E. coli*; wherein said *E. coli* are *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

Claims 91, 93-96 and 124-126 are directed to methods of making competent *E. coli*, comprising: (a) obtaining *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B; and (b) treating said *E. coli* to make it competent.

Claim 97 is directed to competent *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting

of *E. coli* MM294, DH5α and DH10B. Claims 99-102 and 127-129 are cancelled; however, new claims 131-136 depend from claim 97 and encompass subject matter that is similar to that which was encompassed by claims 99-102 and 127-129.

Jessee describes a method for producing cells of improved competency. *See* Jessee at column 1, lines 10-11. Jessee exemplifies the method by illustrating the transformation of *E. coli* strains RR1 or DH5 with the plasmid pBR322. *See, e.g.*, Jessee at column 7, line 58 through column 9, line 18, and at column 9, lines 20-53.

Under the applicable legal standard for establishing a *prima facie* case of obviousness, there must be some clear and particular evidence indicating that a skilled artisan would have been motivated to combine or modify the cited references. *See Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617. No such evidence has been presented here. The Examiner simply stated that:

> [t]he ordinary skilled artisan would have been motivated to combine these teachings in order to obtain competent cells that could grow faster when used in cloning reactions. It would have been obvious to combine these teachings because the method described by Jessee is for use with bacterial cells, which the cells of *E. coli* strain W represent.

Paper No. 16, pages 9-10.

Applicants respectfully submit that the Examiner's justification for the rejection under § 103 is legally insufficient. There has been no specific and particular evidence presented to indicate why a skilled artisan would have been motivated to obtain rapid growing competent cells. Accordingly, the teachings of Jessee do not support a *prima facie* case of obviousness under § 103.

2. Claims 76-81, 86 and 87

Claims 76-81 depend, directly or indirectly, from claim 75. Claim 75 in its present form is directed to a kit for cloning comprising a container containing *E. coli* lacking endogenous plasmids and having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

Claims 86 and 87 depend from claim 85 which, in its present form, is directed to a composition comprising *E. coli*, wherein said *E. coli* of said composition lack endogenous plasmids and have a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

A *prima facie* case of obviousness cannot be established with respect to claims 76-81, 86 and 87. A *prima facie* case of obviousness requires both (1) specific and particular evidence of a motivation to combine or modify the cited references; and (2) disclosure in the cited references of all of the elements of the claims. *See Rouffet*, 149 F.3d at 1357, 47 USPQ2d at 1457-58, and *Royka*, 490 F.2d at 180 USPQ at 580. As explained above, Jessee cannot establish a *prima facie* case of obviousness with respect to claims 76-81, 86 and 87.

3. Summary

As noted in more detail above, a *prima facie* case of obviousness has not been established in view of the cited art. *E. coli* strain W in view of Jessee does not render any of the currently presented claims, including the newly added claims, obvious. Accordingly,

Applicants respectfully request that rejection of claims 48, 49, 51, 55-57, 69, 70, 72-74, 76-81, 86, 87, 91, 93-97, 99-102, 106-108, 115-117 and 124-129 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

C. E. coli Strain W in View of Trevors and Jessee

Claims 50, 64-68, 71, 92, 98 and 112-114 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over "applicant's admissions concerning *E. coli* strain W" in view of Trevors, and further in view of Jessee. *See* Paper No. 16, page 10. Applicants respectfully traverse this rejection.

Claim 50 is directed to the method of claim 48 (*see* above), wherein said *E. coli* are *E. coli* strain W or strain C; and wherein said *E. coli* do not contain endogenous plasmids.

Claims 64-68 and 112-114 are directed to methods of producing *E. coli* for cloning, comprising: (a) obtaining *E. coli* having endogenous plasmids and having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B; and (b) curing said *E. coli* of endogenous plasmids.

Claim 71 is directed to the method of claim 69 (*see* above), wherein said *E. coli* are *E. coli* strain W or strain C, and wherein said *E. coli* do not contain endogenous plasmids.

Claim 92 is directed to the method of claim 91 (*see* above), further comprising the step of curing said *E. coli* of endogenous plasmids.

Claim 98 was directed to competent *E. coli* having a growth rate that is at least 5% greater than the growth rate of a reference microorganism selected from the group consisting

of *E. coli* MM294, DH5α and DH10B; wherein said competent *E. coli* are produced according to the method of claim 92 (*see* above). Claim 98 has been cancelled; however, new claims 131-136 encompass subject matter that is similar to that which was encompassed by claim 98.

A *prima facie* case of obviousness has not been established with respect to any of the currently presented claims because there has not been any specific and particular evidence set forth to indicate that a skilled artisan would have been motivated to modify or combine the cited references to arrive at the claimed invention. The Examiner has simply stated that:

> The ordinary artisan would have been motivated to combine these teachings in order to obtain competent cells lacking endogenous plasmids that could interfere with cloning/transformation reactions (i.e., plasmid recovery). It would have been obvious to combine these teachings because the method described by Jessee is for use with bacterial cells, which the cells of *E. coli* strain W in view of Trevors represent.

Paper No. 16, page 10.

The Examiner, however, has not pointed to anything in particular which indicates the desirability of obtaining competent cells lacking endogenous plasmids. There is nothing in either Jessee or Trevors that indicates that endogenous plasmids "could interfere with cloning/transformation reactions." Thus, a *prima facie* case of obviousness has not been established. *E. coli* strain W in view of Trevors and Jessee does not render any of the currently presented claims, including the newly added claims, obvious. Accordingly, Applicants respectfully request that the rejection of claims 50, 64-68, 71, 92, 98 and 112-114 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

D. E. coli Strain W in View of Jessee and Nathan

Claims 58, 59, 61-63 and 109-111 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over "applicant's admissions concerning *E. coli* strain W" in view of Jessee, and further in view of Nathan *et al.*, U.S. Patent No. 5,914,390 (hereinafter "Nathan"). *See* Paper No. 16, page 11. Applicants respectfully traverse this rejection.

Claims 58, 59, 61-63 and 109-111 are directed to methods of producing a protein or peptide, comprising: (a) obtaining competent *E. coli*; (b) transforming into said competent *E. coli* a vector containing a gene encoding a protein or peptide; and (c) culturing said transformed *E. coli* under conditions that cause said transformed *E. coli* to produce said protein or peptide; wherein said *E. coli* are *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

A *prima facie* case of obviousness has not been established with respect to claims 58, 59, 61-63 and 109-111 because there has not been any specific and particular evidence set forth to indicate that a skilled artisan would have been motivated to modify or combine the cited references to arrive at the claimed invention.

Jessee has already been discussed in detail above. Nathan describes the use of certain "protective agents" to improve the yields of recombinant proteins by preventing the degradation and/or modification of recombinant proteins during the purification process. *See* Nathan at column 2, lines 2-9. Nathan exemplifies the production of human insulin-like growth factor binding protein 3 (IGFBP-3) from an *E. coli* host strain. *See* Nathan at column 5, line 50 through column 6, line 42. Nathan does not indicate or suggest that the

agents or methods described therein can or should be used in the production of recombinant proteins from rapid growing *E. coli*.

The Examiner has not presented any specific evidence suggesting that a skilled artisan would have been motivated to use *E. coli* strain W or any other rapid growing *E. coli* in the methods of Nathan or to combine the methods of Nathan with the methods of Jessee. The Examiner has simply stated that:

> The ordinary skilled artisan would have been motivated to combine the teachings in order to produce polypeptides in a more timely fashion, owing to the faster growth properties of *E. coli* strain W. It would have been obvious to combine these teachings because the method of Nathan is designed for use with bacterial cells, which are represented by *E. coli* strain W.

Paper No. 16, page 11.

The Examiner, however, has not pointed to anything in particular which indicates the desirability of producing polypeptides in rapid growing *E. coli*. There is nothing that indicates that polypeptides could or should be produced in a "more timely fashion." Thus, a *prima facie* case of obviousness has not been established. *E. coli* strain W in view of Jessee and Nathan does not render any of the currently presented claims, including the newly added claims, obvious. Accordingly, Applicants respectfully request that the rejection of claims 58, 59, 61-63 and 109-111 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

E. E. coli Strain W in View of Trevors, Jessee and Nathan

Claim 60 was rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over "applicant's admissions concerning *E. coli* strain W" in view of Trevors, and further in view

of Jessee and Nathan. *See* Paper No. 16, page 12. Applicants respectfully traverse this rejection.

Claim 60 is directed to the method of claim 58 (*see* above), wherein said *E. coli* are *E. coli* strain W or strain C, and wherein said *E. coli* do not contain endogenous plasmids.

A *prima facie* case of obviousness has not been established with respect to claim 60 because there has not been any specific and particular evidence set forth to indicate that a skilled artisan would have been motivated to modify or combine the cited references to arrive at the claimed invention. The Examiner has simply provided the following explanation for the rejection:

> The ordinary skilled artisan would have been motivated to combine the teachings in order to produce polypeptides in [a] strain lacking endogenous plasmids, such as those described by Trevors modified *E. coli* strain W, so that the endogenous plasmids would not interfere with [the] maintenance of the plasmid of interest. It would have been obvious to combine these teachings because the method of Nathan is designed for use with bacterial cells, which are represented by the Trevors modified *E. coli* strain W.

Paper No. 16, page 12.

Applicants respectfully submit that this explanation is legally insufficient to establish a *prima facie* case of obviousness. There has been no specific evidence presented that indicates the advantages associated with producing polypeptides in a bacterial strain that lacks endogenous plasmids. Neither Trevors, Jessee nor Nathan indicate or suggest that endogenous plasmids "would interfere with [the] maintenance of the plasmid of interest." Thus, a *prima facie* case of obviousness has not been established. *E. coli* strain W in view of Trevors, Jessee and Nathan does not render any of the currently presented claims,

including the newly added claims, obvious. Accordingly, Applicants respectfully request that the rejection of claim 60 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

42. (Twice amended) Isolated *E. coli* lacking endogenous plasmids and having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

47. (Twice amended) The isolated *E. coli* of claim 42, wherein said isolated *E. coli* have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

48. (Twice amended) A method of cloning, comprising:

(a) obtaining competent *E. coli*;

(b) transforming said competent *E. coli* with at least one vector;

(c) selecting transformed *E. coli* containing said [a reference] at least one vector; and

(d) culturing said transformed *E. coli*;

wherein said *E. coli* are *E. coli* having a growth rate that is at least 5% greater than the growth rate of at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

50. (Twice amended) The method of claim 49, wherein said *E. coli* do not contain endogenous [vectors] plasmids.

51. (Once amended) The method of claim 48, further comprising the step of isolating said [recombinant] vector from said transformed *E. coli*.

57. (Twice amended) The method of claim 48, wherein said *E. coli* have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

58. (Twice amended) A method of producing a protein or peptide, comprising:

(a) obtaining competent *E. coli*;

(b) transforming into said competent *E. coli* a vector containing a gene encoding a protein or peptide; and

(c) culturing said transformed *E. coli* under conditions that cause said transformed *E. coli* to produce said protein or peptide;

wherein said *E. coli* are *E. coli* having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

63. (Twice amended) The method of claim 58, wherein said *E. coli* have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

64. (Twice amended) A method of producing *E. coli* for cloning, comprising:

(a) obtaining *E. coli* having endogenous plasmids and having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B; and

(b) curing said *E. coli* of endogenous plasmids.

68. (Twice amended) The method of claim 64, wherein said *E. coli* have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

69. (Twice amended) A method of transforming *E. coli*, comprising:

(a) obtaining competent *E. coli*;

(b) incubating said *E. coli* in the presence of one or more vectors under conditions which cause said one or more vectors to be taken up by said *E. coli*; and

(c) culturing said *E. coli*;

wherein said *E. coli* are *E. coli* having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

74. (Twice amended) The method of claim 69, wherein said *E. coli* have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of MM294.

75. (Twice amended) A kit for cloning comprising a container containing *E. coli* lacking endogenous plasmids and having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

79. (Twice amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] are competent.

80. (Twice amended) The kit of claim 79, wherein said *E. coli* [contained within said kit] are chemically competent.

81. (Twice amended) The kit of claim 79, wherein said *E. coli* [contained within said kit] are electrocompetent.

82. (Twice amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] have a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294.

83. (Twice amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] have a growth rate that is at least 5% greater than the growth rate of *E. coli* DH5α.

84. (Twice amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

85. (Twice amended) A composition comprising *E. coli*, wherein said *E. coli* [of said composition] lack endogenous plasmids and have a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B.

88. (Twice amended) The composition of claim 85, wherein said *E. coli* [of said composition] have a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294.

89. (Twice amended) The composition of claim 85, wherein said *E. coli* [of said composition] have a growth rate that is at least 5% greater than the growth rate of *E. coli* DH5α.

90. (Twice amended) The composition of claim 85, wherein said *E. coli* [of said composition] have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

91. (Twice amended) A method of making competent *E. coli,* comprising:

(a) obtaining *E. coli* having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B; and

(b) treating said *E. coli* to make it competent.

92. (Twice amended) The method of claim 91, further comprising the step of curing said *E. coli* of endogenous [vectors] plasmids.

96. (Twice amended) The method of claim 91, wherein said *E. coli* have a growth rate that is [5-200%] 5 to 200% greater than the growth rate of *E. coli* MM294.

97. (Twice amended) [Competent] *E. coli* having a growth rate that is at least 5% greater than the growth rate of [a reference] at least one microorganism selected from the group consisting of *E. coli* MM294, DH5α and DH10B, wherein said *E. coli* has been made competent [; wherein said competent *E. coli* are produced according to the method of claim 91].

118. (Once amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] have a growth rate that is at least 25% greater than the growth rate of *E. coli* MM294.

119. (Once amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] have a growth rate that is at least 50% greater than the growth rate of *E. coli* MM294.

120. (Once amended) The kit of claim 75, wherein said *E. coli* [contained within said kit] have a growth rate that is at least 100% greater than the growth rate of *E. coli* MM294.

121. (Once amended) The composition of claim 85, wherein said *E. coli* [of said composition] have a growth rate that is at least 25% greater than the growth rate of *E. coli* MM294.

122. (Once amended) The composition of claim 85, wherein said *E. coli* [of said composition] have a growth rate that is at least 50% greater than the growth rate of *E. coli* MM294.

123. (Once amended) The composition of claim 85, wherein said *E. coli* [of said composition] have a growth rate that is at least 100% greater than the growth rate of *E. coli* MM294.

Claims 44, 98-102 and 127-129 are sought to be cancelled.

Claims 130-149 are sought to be added.